

REMARKS

Initially, Applicants would like to thank the Examiner for granting a telephone interview on January 4, 2005. During this interview, Applicants discussed certain rejections raised in the Non-final Office Action dated December 3, 2003, ("Non-final Office Action"), the Final Office Action dated September 8, 2004 ("Final Office Action"), and the Advisory Action dated December 3, 2004 ("Advisory Action"). The Examiner requested that Applicants' discussion be presented in writing. To meet the Examiner's request, Applicants file this supplemental reply to the Final Office Action.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-9 and 23-36, drawn to a discrimination primer and a kit including the discrimination primer, for failing to meet the written description requirement.

According to her,

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention since the newly added limitation 'unlabelled' discrimination primer [to independent claims 1 and 23] has no support in the specification." (See the Final Office Action, the paragraph bridging pages 5 and 6.)

Applicants would like to point out that, contrary to the Examiner's position, the Specification provides support for the limitation. For example, it has disclosed two actually prepared discrimination primers, R11-1-3mis18 (SEQ ID NO: 2) and RM11-1-3mis18 (SEQ ID NO: 3). These two primers were not labeled or unlabeled, i.e., not linked to a traceable constituent. See page 8, lines 5-11.

It appears to be the Examiner's position that the phrase "unlabeled discrimination primer" is not explicitly described in the specification. Applicants note that the discrimination primer must be unlabeled for one to practice the instant invention. To illustrate this point, Applicants have attached Exhibit 1, which was filed with the response mailed July 16, 2003. Shown in Exhibit 1A is an unlabeled discrimination primer. This discrimination primer, together with a

labeled amplification primer, allows one to amplify a polymorphism-containing target nucleic acid using the PCR. See Exhibit 1B. After the PCR, one can (1) affix one end of the amplified nucleic acid onto a substrate via the first binding member of the unlabeled discrimination primer and a second binding member already affixed on a substrate, and (2) detect the bound target nucleic acid via the labeled amplification primer incorporated into the other end of the amplified target nucleic acid. **If a discrimination primer were labeled, such as the one shown in Exhibit 1C, one would not be able to detect the bound target nucleic acid since free labeled discrimination primers, which also bind to the substrate, create a very high background.** Thus, a skilled artisan would have understood that the discrimination primer must be unlabeled even if this limitation is not explicitly described in the Specification.

In this connection, Applicants would like to remind the Examiner that

If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., Vas-Cath, 935 F.2d at 1563, 19 USPQ2d at 1116; Martin v. Johnson, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient"). See MPEP 2163.II.A.3

As "a skilled artisan would have understood" that the discrimination primer must be unlabeled, "then the adequate description requirement is met."

For the remarks set forth above, Applicants submit that the claims at issue meet the written description requirement

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-9 and 23-36 for obviousness on two grounds. Applicants respectfully traverse each ground:

I

In the Non-final Office Action, the Examiner rejected claims 1-4, 6-8, 23-26, 30, and 32-36 as being obvious over U.S. Patent No. 6,156,503 to Drazen et al. ("Drazen") in view of

Ugozzoli et al. (GATA, 1992, Vol. 9(4), pp. 107-112; "Ugozzoli"). She maintained the rejection in the Final Office Action and Advisory Action. Applicants respectfully traverse and will discuss claim 1 first.

Claim 1 covers a discrimination primer for PCR amplification that includes, among others, a mismatch at the penultimate position from its 3' end and a first binding member, which binds to a second binding member. Ugozzoli teaches a primer for primer extension having a 5' X portion that is complementary to an immobilized, pre-selected nucleic acid sequence. According to the Examiner, the 5' X portion and the pre-selected nucleic acid sequence are equivalent to the first and second binding members, respectively. The Examiner contended that, in view of Drazen's teaching of an amplification primer that has a penultimate mismatch, a combination of the two references would suggest the claimed discrimination primer for PCR amplification.

In the response to the Non-final Office Action, Applicants pointed out that Ugozzoli's teaching, limited to primer extension, is not necessarily applicable to PCR amplification. More specifically, since the specificity requirement for a PCR amplification primer is much stricter than for an extension primer, a functional extension primer may not work as a PCR amplification primer to generate specific amplification products. Thus, one skilled in the art would not (i) have a reasonable expectation of success or (2) have been motivated to combine Ugozzoli's teachings on extension primers and Drazen's teachings in the manner proposed by the Examiner to make a discrimination primer of claim 1, which is limited to PCR primers only. To support this argument Applicants submitted a Declaration by Dr. Wang showing that, indeed, a primer as suggested by Drazen and Ugozzoli did not work as a PCR amplification primer.

Nonetheless, in the Final Office Action, the Examiner maintained the rejection. It appeared to be her position that (1) claim 1 covers extension primers, and (2) the Declaration was submitted to present an unexpected result on a specific PCR primer not recited in claim 1 (i.e., one containing SEQ ID NO: 2) and therefore was not commensurate in scope with claim 1.

In the response to the Final Office Action dated November 8, 2004, Applicants pointed out that (1) claim 1 does not cover extension primers, and (2) the Declaration was submitted to

support that one skilled in the art would not have a reasonable expectation of success or have been motivated to apply Ugozzoli's teaching on an extension primer to a PCR amplification primer, e.g., that covered by claim 1.

Yet, Applicants' arguments were apparently not considered as evidenced by the Examiner's silence on these arguments in the Advisory Action dated December 3, 2004. As a result, she maintained the rejection.

During the above-mentioned interview, Applicants' counsel reiterated (1) the different technical requirements for an extension primer and a PCR primer and (2) the intended purpose of the Declaration. The Examiner agreed to reconsider this application and requested that the arguments be presented in a supplemental response.

In view of above remarks, Applicants submit that claim 1 is not rendered obvious by Drazen and Ugozzoli. Claim 23 covers a kit that contains the discrimination primer of claim 1. For the same reasons set forth above, it is also non-obvious over these two references. So are claims 2-4, 6-8, 24-26, 30, and 32-36, all of which depend from claims 1 and 23.

II

In the Non-final Office Action, the Examiner also rejected claims 5, 9, 27-29, and 31, which depend from claim 1 or 23, as being obvious over Drazen in view of Ugozzoli and U.S. Patent No. 6,383,742 to Drmanac et al. ("Drmanac").

In the response to the Non-final Office Action, Applicants pointed out: (i) the three cited references would suggest a labeled primer, and (ii) the discrimination primer recited in claim 1 and the first primer recited in claim 23 are unlabeled. Thus, the three references teach away from claims 1 and 23, as well as claims 5, 9, 27-29, and 31 depending from them.

In the Final Office Action, the Examiner countered that "there is a second primer cited in claim 28, which is labeled at the 5' end. ... Thus the combination of the reference renders claims [5, 9, 27-29, and 31] obvious and the rejection is maintained." In the subsequent response, Applicants pointed out that even if the prior art would have suggested a labeled second primer, they would have not suggested a labeled first primer.

Again, in the Advisory Action, the Examiner was silent on Applicants' arguments. Apparently, she did not consider them. At the Examiner's request, Applicants have filed this supplemental response to reiterate the arguments.

In addition, Applicants would like to clarify that the second primer recited in claim 28 differs from the first/discrimination primer recited in claim 1 or 23. In fact, claim 28 covers a kit containing, among others, two distinct primers: (1) a first unlabelled primer identical to that claimed in claim 1, i.e., an unlabelled amplification primer; and (2) a second primer identical to the above-mentioned amplification primer. As discussed in the "Rejection under 35 U.S.C. §112, first paragraph" section above, these two primers, together, allow one to amplify a polymorphism-containing target nucleic acid using the PCR. Also as discussed therein, the second/amplification primer is labeled while the discrimination/first primer is unlabelled. Apparently, the Examiner has mistaken this labeled second/amplification primer for the unlabelled first/ discrimination primer. As the three cited references do not suggest an unlabeled first/discrimination primer, as required in claim 1 or 23, they do not render claims 1 and 23 obvious. Neither does it render obvious claims 5, 9, 27-29, and 31, which depend from claim 1 or 23.

CONCLUSION

Applicants submit that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that meets the written description requirement and is non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

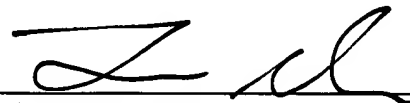
Applicant : Harn-Jing Terng, et al
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Page : 13 of 13

Attorney's Docket No.: 12674-003001

Enclosed is a \$60 check for the Petition for Extension of Time fee. Please apply any other charges to deposit account 06-1050, referencing the attorney docket 12674-003001.

Respectfully submitted,

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